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产品名称：BEZ235 (Tosylate)
产品别名：Dactolisib Tosylate

生物活性：

Description

Dactolisib Tosylate (BEZ235 Tosylate) is a dual PI3K and mTOR kinase inhibitor with IC50 values of 4, 75, 7, 5 nM for PI3Kα, β, γ, δ, respectively. Dactolisib Tosylate (BEZ235 Tosylate) inhibits mTORC1 and mTORC2.

IC_{50} & Target

p110α	p110α-H1047R	p110α-E545K	p110γ	p110δ
4 nM (IC_{50})	4.6 nM (IC_{50})	5.7 nM (IC_{50})	5 nM (IC_{50})	7 nM (IC_{50})
p110β	mTOR	mTORC1	mTORC2	Autophagy
75 nM (IC_{50})	20.7 nM (IC_{50})			

In Vitro

Dactolisib (BEZ235) is an imidazo[4,5-c]quinoline derivative that inhibits PI3K and mTOR kinase activity by binding to the ATP-binding cleft of these enzymes. The IC_{50}s for PI3Kα, β, γ, δ are 4, 75, 7, 5 nM, respectively. It is also found to be as active against the mutant $PI3K\alpha^{E545K}$ or $PI3K\alpha^{H1047R}$ with IC_{50}s of 5.7 and 4.6 nM, respectively. In human tumor cell lines, it is able to effectively and specifically block the dysfunctional activation of the PI3K pathway, inducing G1 arrest. PTEN-null cell lines PC3M and U87MG shows a dose-dependent reduction in cell proliferation when treated with increasing concentrations of Dactolisib (BEZ235), with an average GI_{50} of 10 to 12 nM[1].

In Vivo

Dactolisib (BEZ235) is well tolerated, displays disease stasis when administered orally, and enhances the efficacy of other anticancer agents. At a dose of 50 mg/kg, Dactolisib (BEZ235) appears rapidly in plasma with a C_{max} of 1.68 μM at 0.5 h and a C_{24h} of 0.03 μM[1].

Solvent&Solubility

In Vitro:

DMSO : 34 mg/mL (52.98 mM; Need ultrasonic and warming)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions (Solvent / Mass / Concentration)	1 mg	5 mg	10 mg
1 mM	1.5583 mL	7.7913 mL	15.5826 mL
5 mM	0.3117 mL	1.5583 mL	3.1165 mL
10 mM	0.1558 mL	0.7791 mL	1.5583 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO →90% corn oil

	Solubility: ≥ 1 mg/mL (1.56 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (1.56 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 10.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Maira SM, et al. Identification and characterization of NVP-BEZ235, a new orally available dual phosphatidylinositol 3-kinase/mammalian target of rapamycin inhibitor with potent in vivo antitumor activity. Mol Cancer Ther, 2008, 7(7), 1851-1863.

实验参考：

Animal Administration	Mice: The NVP-Dactolisib (BEZ235) powder is dissolved in NMP on sonication, and the remaining volume of polyethylene glycol 300 is added to a concentration of 5 mg/mL. The application volume is 10 mL/kg. For analytics, frozen tissues are minced and then homogenized in an equal volume of ice-cold PBS and centrifugation, supernatants are analyzed. Samples are then eluted with a linear gradient of 10% to 90% (v/v) acetonitrile in water containing 0.05% (v/v) trifluoroacetic acid over a period of 20 min at a flow rate of 1 mL/min. The compounds are detected by UV absorbance at 340 nm, and concentrations are determined by the external standard method using peak heights[1].
References	[1]. Maira SM, et al. Identification and characterization of NVP-BEZ235, a new orally available dual phosphatidylinositol 3-kinase/mammalian target of rapamycin inhibitor with potent in vivo antitumor activity. Mol Cancer Ther, 2008, 7(7), 1851-1863.